CLINICAL VIGNETTE

A Rare and Fatal Diagnosis in a Previously Healthy Fifty-One-Year-Old Male

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A 51-year-old previously healthy male presented to his primary care physician with confusion and memory loss of three weeks duration. He also complained of progressively worsening fatigue. His wife had noticed that he was missing business appointments and becoming increasingly forgetful, which was affecting his ability to function normally. His physician did not note any significant neurologic findings on physical exam and ordered an MRI of his brain. He was referred to the Emergency Department to expedite the work-up of his constellation of findings. In the Emergency Department, a lumbar puncture was performed and he was admitted with a working diagnosis of possible encephalitis.

On admission he denied headache, seizures, head trauma, loss of consciousness, vision changes, fever, or chills. He had no numbness, sensory loss, or weakness. The patient and family denied any sick contacts, a history of remote or recent international travel. He had no history of animal, mosquito, or tick exposure. His most recent travel was to New York on a business trip a month prior. He denied prior surgery or any blood transfusions and his family history was not significant for any early onset degenerative neurologic conditions, dementia or inherited disorders of metabolism. He was married with three healthy children and worked as a real estate investor. He was a lifelong non-smoker with occasional alcohol use and no illicit or recreational drug use.

Physical examination revealed a well-nourished male with normal vital signs, normal pupillary response, and no meningismus. He was awake, alert, oriented to place, time, and person, but tended to repeat himself after each sentence. His cranial nerve exam was intact. He had no sensory or motor deficits and on evaluation of his cerebellar function had slowed coordination but an intact finger to nose response with some mild intention tremor bilaterally. His deep tendon reflexes were decreased and his speech fluent but slowed. Laboratory studies were all unremarkable. Gadolinium enhanced brain MRI revealed cortical hyperintensity in the frontal and bilateral parietal lobes. Lumbar puncture was significant for an opening pressure of 20 cm, no pleocytosis, normal protein, and no evidence of infection. A Meningitis/Encephalitis panel (PCR detection of 14 CNS pathogens) was negative.

Electroencephalogram showed periodic triphasic sharp waves in bifrontal electrodes and occasionally in occipital electrodes.

Given non-specific findings, he was discharged the next day to follow up with his neurologist as an outpatient. Over the ensuing month, the patient continued to deteriorate with increasing confusion and new onset myoclonic jerking. He returned to the hospital after a witnessed tonic-clonic seizure. On exam, he was confused with no recollection of the seizure event and could not provide any history. Neurological exam was significant for inability to recognize his family members and myoclonus at rest that became more pronounced when he was awake and moving. He had increased tone in extremities. He improved with intravenous levetiracetam and valproic acid to treat the seizures and myoclonic jerks. On repeat lumbar his cerebrospinal fluid 14-3-3 protein was positive and a RT QuIC assay was positive for sporadic Creutzfeld-Jakob disease. The patient was admitted to the medical floor where he continued to worsen. Over the ensuing days, we noted deterioration in his mental status and increased myoclonic activity. Eventually, he was unable to swallow and given his altered mental status was a high aspiration risk. The family decided against a feeding tube and after discussions with the medical team decided on inpatient hospice care. The patient expired three days later.

Discussion

This case illustrates a rare case of Sporadic Creutzfelt Jakob Disease (CJD) that occurs in 1 in a million population per year worldwide.[1] The infrequency with which it is encountered especially in a community hospital setting makes it a formidable diagnostic challenge. The rare neurodegenerative disease, CJD, is still the most frequent human prion disease that progresses rapidly once clinical symptoms appear. [2] There is no gender predilection, and age of onset is usually the fifth decade. It is usually fatal within one year of diagnosis.

Our patient had the classic clinical signs and two cardinal features of CJD–rapidly progressive mental deterioration and persistent myoclonus. Other hallmarks were triphasic waves on EEG and confirmatory CSF protein markers 14-3-3 protein. This test is specific but less sensitive for a diagnosis of CJD.

There is a relatively new test, RT QuIC (real time quaking induced conversion) assay of CSF and nasal brushing specimens that is valuable in diagnosing CJD. [3] It has a quick

turnaround time of three days and was positive in our case. It is also a very sensitive and specific test for CJD. This test is particularly important for early and accurate diagnosis of human prion diseases such as CJD because prions can be deadly, transmissible, (but not contagious) and unusually resistant to decontamination.

The Centers for Disease Control's Diagnostic Criteria for sporadic Creutzfeldt - Jakob disease (CJD) is definitively confirmed when diagnosed by standard neuropathological techniques. These include detection of protease-resistant Prion Protein or scrapie-associated fibrils by neuropathology, immunochemical technique, and/or Western blot. This was not possible in our case as the family declined brain biopsy or autopsy. However, the diagnosis is highly probable[4, 5] based on his rapidly progressive dementia, and at least two out of the following four clinical features: myoclonus, visual or cerebellar signs, pyramidal or extrapyramidal signs and akinetic mutism. Our patient demonstrated at least three of these clinical findings. Another important component of the diagnosis is a positive result on at least one of the following laboratory tests: A typical EEG (periodic sharp wave complexes) during an illness of any duration; and/or a positive 14-3-3 cerebrospinal fluid (CSF) assay in patients with a disease duration of less than 2 years and/or a Magnetic resonance imaging (MRI) high signal abnormality in the caudate nucleus and/or putamen on diffusion-weighted imaging (DWI) or fluid attenuated inversion recovery (FLAIR). The last criteria was also present in our patient.

A useful list of differential diagnoses for the clinical presentation of rapidly progressive dementia include:[6] Alzheimer's disease, dementia with Lewy Bodies, frontotemporal dementia, meningoencephalitis, corticobasal degeneration,[7] progressive supranuclear palsy,[8] Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy **(**CADASIL), and paraneoplastic encephalomyelitis.

Although sCJD is not curable and there is no treatment currently available, it is vital for community hospitalists to make an early and accurate diagnosis as some of the conditions often confused with sCJD like viral or bacterial encephalitis are treatable. [9] Accurate and rapid diagnosis allows for patients and their families to make informed treatment decisions about the devastating and progressive nature of the disease and consider palliative options.

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